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ORIGINAL PAPER

Subchondral screw abutment: does it harm the joint cartilage? An in vivo study on sheep tibiae

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Abstract
Purpose Subchondral screw abutment in osteosynthesis of joint fractures is an effective method to achieve sufficient screw grip. In this study we investigated if subchondral screw placement is possible without harming the overlying subchondral plate and joint cartilage iatrogenic.
Materials and Methods A 3.5-mm conventional steel screw was placed in the tibia of ten sheep in distances between 1 and 7 mm beneath the joint cartilage. After a follow up of two and four months, evaluation of the subchondral bone and joint cartilage was performed by means of a histological osteoarthritis score, HRpQCT imaging and determination of the glycosaminoglycan content in the cartilage. The control group was the contralateral knee of the same animal.
Results Histomorphometric evaluation of the Mankin osteoarthritis score revealed no significant difference compared to the control after two ($p = 0.102$) and four months ($p = 0.429$). No correlation between distance of the screw to the cartilage and histological scoring was found ($p = 0.658$, $R2 = 0.04$ after two months and $p = 0.171$, $R2 = 0.18$ after four months). HRpQCT measurements of the subchondral thickness between screw and cartilage after two ($p = 0.05$) and four months ($p = 0.424$) showed no significant difference. Mean glycosaminoglycan content in the treatment group compared to the control after two months ($p = 0.25$) and four months ($p = 0.523$) was not significant different.
Conclusion In conclusion subchondral screw abutment did not damage the joint cartilage after a two- and four-month follow up in this sheep model.

Keywords Osteoarthritis · Posttraumatic osteoarthritis · Cartilage · Subchondral plate · Subchondral bone · Screw osteosynthesis

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Purpose

Osteosyntheses of intra-articular joint fractures require a stable fixation to prevent secondary displacement. Particularly in osteoporotic fractures with inferior bone stock, screw anchorage is even more difficult to achieve and maintain. The simplest method to achieve better screw grip in intra-articular fractures is screw abutment in the subchondral cortical bone. In the field of periarticular correction osteotomies, such as the high tibial osteotomie (HTO), subchondral screw abutment is also commonly used (Fig. 1).

When placing implants close to the joint cartilage one has to consider the impact of subchondral metalwork on the biomechanics and homeostasis of the subchondral bone, subchondral plate and overlying joint cartilage. It is a matter of fact that subchondral sclerosis leads to progression of cartilage damage as observed in the pathogenesis of osteoarthritis [1–5]. The function of the trabecular bone as shock absorber for the joint cartilage decreases [6, 7]. Higher shear stresses within the cartilage are generated through the hardening of the bony bottom chord and increase the damage of the cartilage [1, 8]. Implants anchored in this region also might harden the subchondral bone due to their presence or through remodelling of the bone as reaction to the impact.

In this study we hypothesized that subchondral screw abutment leads to subchondral bone alterations resulting in joint cartilage damage and post-traumatic osteoarthritis.

Materials and method

Study design

The right proximal tibiae of mature sheep were used to simulate subchondral screw placement and to investigate the overlying subchondral bone and joint cartilage. The contralateral left proximal tibiae served as the untreated control site. Region of interest number 1 (ROI 1) was defined as the weight bearing region of the lateral proximal tibial joint surface and ROI 2 as the weight bearing area of the medial tibial joint surface.

Evaluation was performed by means of a macroscopic osteoarthritis score, according the International Cartilage Repair Society (ICRS) [9] and a modified microscopic osteoarthritis score, related to Mankin et al. [10]. Microscopy and high-resolution peripheral quantitative computed tomography (HRpQCT) imaging was used to measure subchondral plate thickness. Early cartilage degeneration was investigated by determination of the glycosaminoglycan (GAG) content in the hyaline cartilage.

A short follow up of two months (four animals) and a longer follow up of four months (six animals) were observed. This study was performed in an AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) approved laboratory, according to the Swiss animal welfare regulations and approved by the ethical committee of the canton Graubünden, Switzerland (No. 2012_29).

Animals

Ten skeletally mature female Swiss alpine sheep, aged two to four years, weighting 62 ±5 kg were used. A veterinarian ruled out orthopaedic disorders prior to the start of the study. The sheep were acclimatized to post-surgical conditions at least two weeks prior to surgical intervention. The animals were fed twice a day with silage, hay and straw. They always had free access to drinking water.

Surgery

Surgery was performed under aseptic conditions while the animals were placed under general anaesthesia.

The sheep were sedated with 0.05 mg/kg Detomidine (Domosedan®, Pfizer AG, Zürich, Switzerland) intramuscular while they were still in the stable. Induction was done using

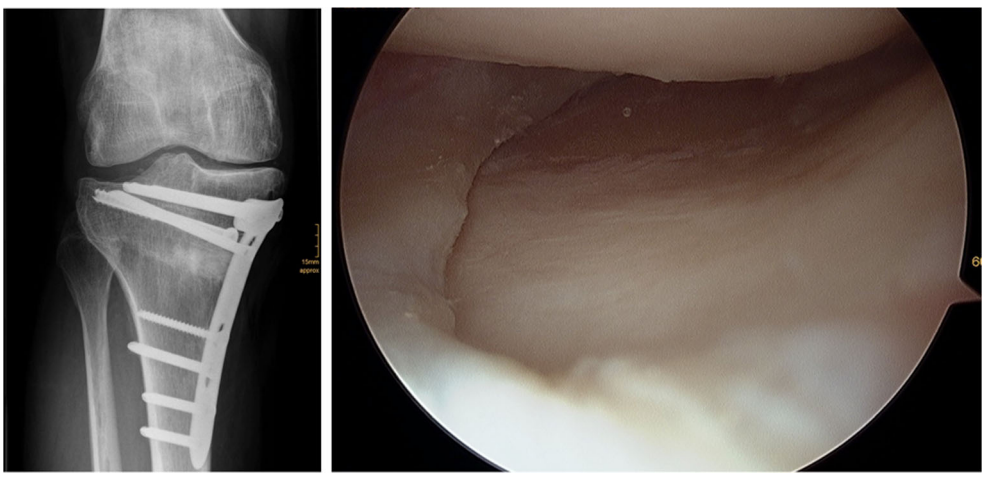

Fig. 1 High tibial osteotomie (HTO) instantaneously underneath the cartilage (*left*) and the corresponding arthroscopic image without macroscopic cartilage alteration (*right*)

0.2 mg/kg Midazolam (Dormicum ®, Hoffmann-La Roche, Basel, Switzerland) and 6 mg/kg Ketamine (Ketasol-100®, Dr. E. Graeub AG, Berne, Switzerland) intravenously. Anesthesia was maintained using approximately 1.5% Isoflurane (Isoflurane Baxter, Baxter AG, Volketswil, Switzerland) in oxygen (oxygen flow rate between 0.6 L/min and 1 L/min). Preemptive analgesia was conducted using 1.4 mg/kg Carprofene (Rimadyl® Rind, Zoetis, Zürich, Switzerland) intravenously and epidural anesthesia with 1 ml Buprenorphine (0.3 mg/ml Temgesic®, Reckitt Benckiser AG, Wallisellen, Switzerland) mixed with 5 ml Lidocaine 2% (Lidocain 2%®, Streuli Pharma AG, Uznach, Switzerland). Each animal received as peri-operative antibiotics 2.2 mg/kg Ceftiofur intravenously (Excenel®, Zoetis, Zürich, Switzerland) one hour before the first surgical incision.

The position of the medial and lateral tibial crest was confirmed with X-ray fluoroscopy (Arcadis Avantic, Siemens, Germany). Medial and lateral stab incisions were performed to allow secure placement of a standardized drill guide (combined aiming device: 130.30, De Puy Synthes Vet., West Chester, PA, USA) beneath the joint line, ranging from 0.5 to 7 mm distance to the joint cartilage (mean 3.7 mm; SD 1.9 mm). A 2.5-mm hole was drilled transverse from medial to the contralateral cortex. Length was measured and a 3.5-mm self-tapping steel screw (De Puy Synthes, Oberdorf, Switzerland) was inserted.

Post-operatively, sheep were kept in individual pens for one day, until they were group housed. Sheep were allowed to fully weight bear immediately after surgery. To alleviate acute post-operative pain, the animals were given 1.4 mg/kg Carprofen (Rimadyl) for five days three times a day, Buprenorphine (Temgesic®) 0.01 mg/kg for 24 hours and Fentanyl-Patches (Durogesic® Matrix) 2 μg/kg/hr for 72 hours. Sutures were removed after 14 days.

Euthanasia and sample processing

After two or four months follow up respectively, animals were euthanized by means of intravenous administration of pentobarbital (300 mg/ml; Esconarkon®, Ad. Us.Vet.). Tibiae of both knee joints were harvested immediately after euthanasia.

ICRS score

Macroscopic evaluation according the ICRS score was preformed within 30 minutes after euthanasia.

HRpQCT

Prior to CT scanning the screw was gently removed from the right tibiae to prevent the occurrence of metal streak artefacts. The fresh, unfixed proximal tibiae including the untreated control sites were scanned at an isotropic resolution of 82 μm using a HRpQCT (XtremeCT, SCANCO Medical AG, Brüttisellen, Switzerland) executed at 60 kVp, 900 μA and using an integration time of 200 ms. The CT scan of the control side was mirrored in the mediolateral plane and registered to its corresponding right tibia in order to evaluate the same ROI in both tibiae. ROIs were defined in the right tibiae: rectangles of 10×6 mm were aligned along the screw axis and placed in the lateral and medial load bearing areas (Fig. 2). The subchondral plate was first roughly separated from trabecular bone using an automated contouring procedure and in a second step the volume of the subchondral plate was evaluated using a threshold of 745 mgHA/cm^3. Lastly, the calculated subchondral plate volume was divided through the base area of the ROI to obtain the average subchondral plate thickness in each ROI.

Histology

All bones were cut in half along a wooden pin, which was placed into the former screw location. The preparation of the contralateral untreated joint oriented on anatomical landmarks to reproduce a similar cutting plane.

Samples were placed in 70% ethanol to dehydrate and embedded in LR-white raisin. Using a polycut sledge microtome

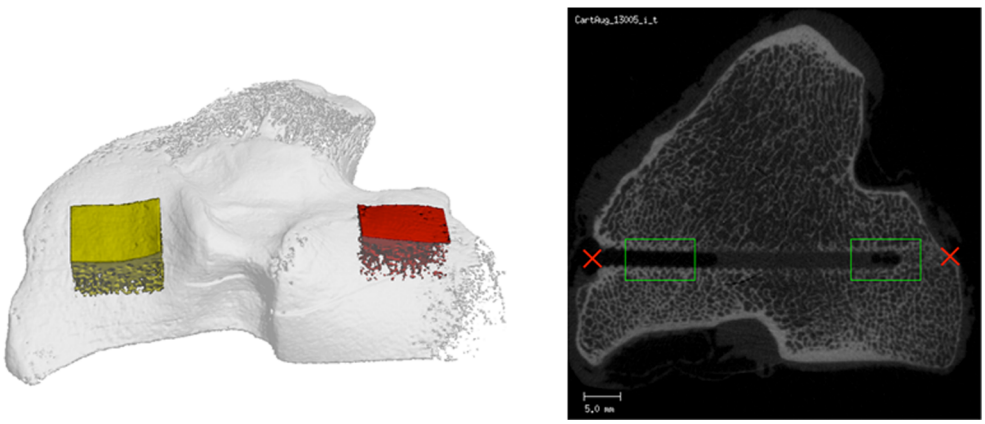

Fig. 2 HRpQCT: Three-dimensional simulation of the subchondral bony structures, based on the calculations within the ROIs (*left*). Rectangles of 10x6 mm aligned along the screw axis and placed in the lateral and medial load bearing areas (*right*)

two slices per sample with a distance of 1000 μm were cut and stained with Giemsa-Eosin and Safranin O.

For histological evaluation a modified Mankin scoring system [10] (Table 1) was used to objectivize the surface constitution of the hyaline cartilage, the tidemark, cell number and formation and content of proteoglycan [11]. Sclerosis of the subchondral bone was evaluated by measuring its thickness at the ROIs. A certified veterinarian pathologist and an orthopaedic surgeon performed scoring using a light optical microscope (Axioplan 2 imaging, Carl Zeiss, Jena, Germany). Additionally, the average distance between screw and cartilage was measured for each ROI.

Biochemistry

At each ROI an osteochondral sample was harvested with a 4-mm diameter biopsy punch. Bone was completely removed from the biopsy. Samples were digested in proteinase K and measurement of sulfated glycosaminoglycan (GAG) using 1.9-dimethylmethylene blue (DMMB) assay (Sigma, Buchs, Switzerland). Samples were normalized to DNA content (PicoGreen assay, Invitrogen, Zug, Switzerland).

Table 1 Modified Mankin [10] score

Findings	Score	Description
I. Cartilage structure		
Normal	0	Matrix/surface normal architecture
Surface reaction	1	Superficial zone intact, edema (increased matrix thickness) and/or superficial fibrillation (abrasion)
Clefts to transitional zone	2	Clefts to transitional zone
Clefts to radial zone	3	Clefts to radial zone
Clefts to calcified zone	4	Clefts to calcified zone
Complete disorganization	5	Complete disorganization
Sum score	5	
II. Cells		
Normal	0	Normal
Zonal disorganization	1	Disorganization of chondrocytes, chondrons, collagen fibrils
Cellular shrinkage	1	Pycnotic nuclei
Hypocellularity	1	Empty lacunae; Reduced number; Dead chondrocytes
Cellular deformity	1	Hypertrophy (increased cell size, cytoplasm); Pupillary unrounding
Inflammation	1	E.g. giant cells
Granulation tissue	1	Fibroblast formation, vessel formation,
Sum score	6	
III. Safranin-O staining		
Normal	0	Compare to control
Slight reduction	1	Depletion of superficial zone
Moderate reduction	2	Depletion including mid zone
Severe reduction	3	Depletion reaching to deep zone
Sum score	3	
IV. Tidemark		
Intact	0	Intact
Crossed by blood vessels	1	Crossed by blood vessels
Disrupted	2	Disrupted
Sum score	2	
Total score	16.0	

Statistics

Statistical evaluation was performed using SPSS (SPSS 22, IBM Corporation, NY, USA). After assessing data distribution (Shapiro-Wilk), paired non-parametric test statistics (Wilcoxon Signed Ranks) were performed to identify differences between treated and untreated control samples regarding histological score. Parametric test statistics (paired samples t-test) were used to identify differences regarding subchondral plate thickness and GAG content ratio. Spearman's correlation coefficient R^2 was used to assess correlations between histological score and screw distance. P-values of < 0.05 were considered significant.

Results

ICRS score

In the two-month group, screw perforation occurred at the medial plateau of one sheep, which was already documented in the surgery report. This ROI was excluded from evaluation. In total, seven out of eight ROIs were evaluated in the two-month group and 12 out of 12 ROIs in the four-month group. No macroscopic changes were found in either group; All of the 19 evaluated samples in the treatment group were scored with 0. The 19 samples of the control group also did not show any pathologic findings and were scored with 0 according the ICRS score.

HRpQCT evaluation

Mean cortical thickness between screw and cartilage after two months was lower (2.129 mm; standard deviation [SD] 2.316 mm) than in the control (3.471 mm; SD 3.526) without significance (p =0.050). After a four-month follow up there was also no significant difference (p =0.424) of the subchondral plate thickness in the treatment group (2.150 mm; SD 1.94 mm) compared to the control group (2.508 mm; SD 2.312 mm).

Histology

Histological scoring revealed a median score of 1 (range 8) for the two-month treatment samples. There was no significant difference ($p = 0.102$) compared to the two-month control samples, which showed a median score of 0 (range 2). Similarly, the four-month treatment samples showed a median

score of 1 (range 3), which was statistically not different (p = 0.429) from the four-month control samples with a median score of 0 (range 3). Only one out of 19 evaluated ROIs revealed a manifest osteoarthritis with severe reduction of Safranin O staining, missing of the tidemark and disruption of the zonal formation in the treatment group.

No correlation between screw distance to cartilage and histological score was found in the two-month group ($p = 0.658$, $R^2 = 0.04$) and four-month group ($p = 0.171$, $R^2 = 0.18$).

Histological measurement of the subchondral plate thickness revealed no significant difference between treatment and control group: mean 710 μm (SD 542 μm) versus mean 752 μm (SD 436 μm) after two months ($p = 0.841$) and mean 232 μm (SD 108 μm) versus mean 295 μm (SD 212 μm) after four months ($p = 0.278$).

Biochemistry

Mean GAG content ratio for the two-month treatment group was 501 (SD 330) and for the two-month control group 948 (SD 703) without significance ($p = 0.245$). Also after four months no significant difference ($p = 0.523$) was observed in GAG content ratio between treatment (298 SD 341) and control groups (236 SD 223).

Discussion

Osteosynthesis failure with loss of reduction is a common complication resulting in post-traumatic osteoarthritis [12–14]. Implant anchorage close to the subchondral plate is an established method to improve the osteosynthesis due to better screw grip in the bone [15, 16].

In this study it was hypothesized that cartilage is damaged when implants come too close to the joint line. Histological osteoarthritis score and biochemical evaluations of the cartilage revealed no significant difference to control samples after two and four months follow up regardless of the distance of the screw to the cartilage (Table 2). Even with the screw tip located instantaneously (<1 mm distance) underneath the cartilage no significant cartilage changes were observed compared to the control (Figs. 3 and 4).

Osteoarthritis usually goes hand in hand with thickening of the subchondral plate and sclerosis of the subchondral trabecular bone. This leads to loss of function of the subchondral bone, which is responsible for buffering axial peak forces transduced through the hyaline cartilage [1]. Histological and HRpQCT images showed a small sclerotic seam around the implant. In HRpQCT imaging sclerosis was defined with a threshold of 745 mgHA/cm3, related to the average value which was measured in the subchondral plate. Compared to the control no significant increase of sclerosis occurred. After two months a tendency of more sclerotic bone above the screw, most likely induced by the periimplant seam, was measured. After four months claculation of the sclerotic bone was on average less than in the control group. In order to validate these contrary HRpQCT results we measured subchondral plate thickness in the histological sections (Fig. 5). The periimplant seam was included in the measurement for the subchondral plate in case screw placement was within the subchondral plate (≤ 1 mm underneath the cartilage; n =3) or the seam was connected with the subchondral plate (Fig. 6). Because of the small sample number (n = 3) no statistical evaluation can be made according to thickening of the subchondral plate when screw placement occurs within 1 mm underneath the cartilage.

It was suspected that the stiff steel screw beneath the cartilage could lead to cartilage tear. According to Kuhn et al. shear forces in the cartilage are generated when a discontinuity in stiffness such as subchondral changes or adjacent implants occur [17]. Fissures or tear of the cartilage were not observed more often than the physiological findings in the control group. According to Armstrong et al. [18] topographical cartilage alterations are physiologic. In their study they examined untreated sheep stifle joints using the Mankin score to show topographical alterations and described slight roughening and fissuring as physiologic. Vanderweerd et al. [19] also advise to take into account prevalent subclinical cartilage defects at the baseline in studies using ovine models.

Another theory for post-traumatic arthritis is the effect of the initial trauma. Martin et al. [20] attribute cartilage degeneration after initial trauma to the release of reactive oxygen species. Several studies investigated subchondral bone marrow oedema after trauma to the joint, so-called bone bruises,

Table 2 Summary of the results

Measure	Two-month treatment	Two-month control	*p*-value	Four-month treatment	Four-month control	*p*-value
Histological score	1 (range 8)	0 (range 2)	0.102	1 (range 3)	0 (range 3)	0.429
Biochemical evaluation: GAG/DNA-ratio	501 (SD 330)	948 (SD 703)	0.245	298 SD 341	236 SD 223	0.523
Subchondral plate thickness in μm (histology)	710 μm (SD 542 μm)	752 μm (SD 436 μm)	0.841	232 μm (SD 108 μm)	295 μm (SD 212 μm)	0.278
Subchondral plate thickness in mm (HRpQCT)	2.129 mm (SD 2.316 mm)	3.471 mm (SD 3.526)	0.050	2.15 mm (SD 1.94 mm)	2.508 mm (SD 2.312 mm)	0.424

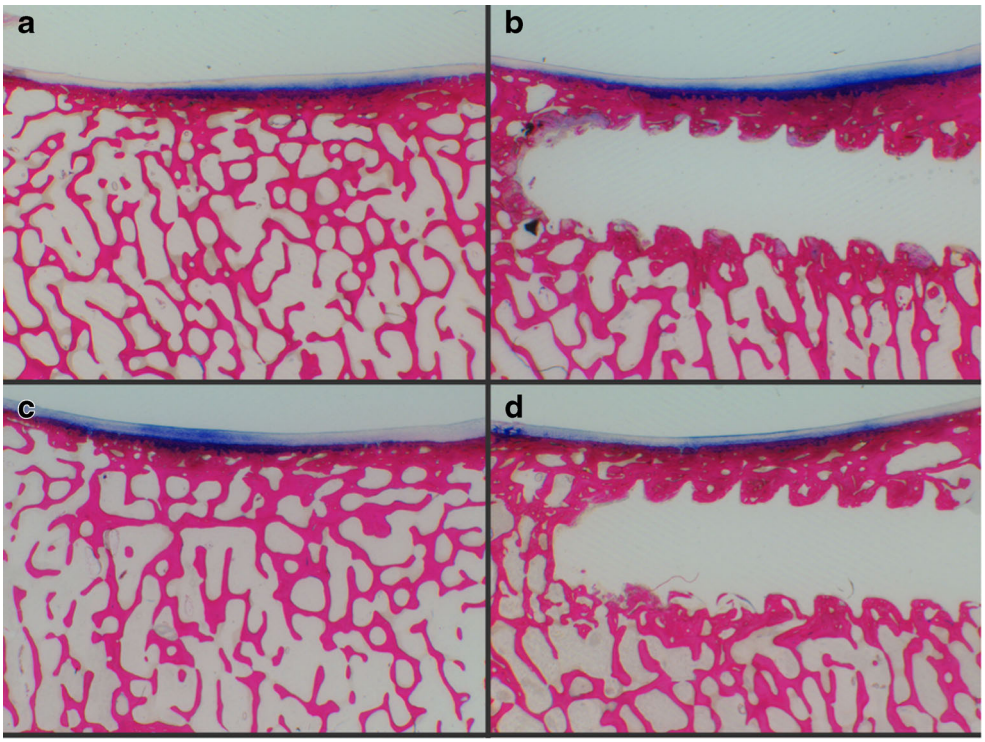

Fig. 3 Histologic sections of screw placement into the subchondral plate (**b** and **c**) and the corresponding control sections (**a** and **c**). All four sections were scored with 0 according the modified Mankin score

and its negative effect on the cartilage [21, 22]. Histological examination of cartilage biopsies taken above normal bone bruises after anterior crus ligament (ACL) rupture revealed degeneration of the chondrocytes and loss of proteoglycan in the articular cartilage. There was necrosis of osteocytes in the subchondral plate, and empty lacunae were visible [22]. The increased oxidative stress on chondrocytes accelerates chondrocyte senescence which decreases the ability of the cells to maintain or restore the tissue [20]. Therefore we analysed if subchondral implant placement can induce an impact to the subchondral bone and the overlying cartilage comparable with a retrograde bone bruise. No magnetic resonance images (MRI) were taken, so that possible initial bone marrow oedema after implanting were not detected. Nevertheless persistent oedema and histological equivalents [22–25], such as microfractures of the trabeculae, bleeding in the fatty marrow and cartilage changes would have been detected in the histology. Such findings were not observed more often in either group. The implant used in this study was a self-tapping screw, inserted after predrilling. Implants inserted with higher forces, e.g. hammering the blade of the proximal femur nail, could possibly generate more subchondral pressure and lead to persistent bone marrow oedema with consecutive cartilage damage. Impaction of the trabeculae could induce an iatrogenic subchondral sclerosis. Also discussed in the literature is the negative effect of heat generation during drilling on cortical bone, which could have biased our investigations [26]. Drilling of the subchondral bone for the use of cartilage regeneration did not show heat necrosis in a canine study histologically [27]. Further reasons for post-traumatic arthritis are residual joint incongruity or preexisting arthritis [28, 29]. For this reason we chose a no fracture model for this study in

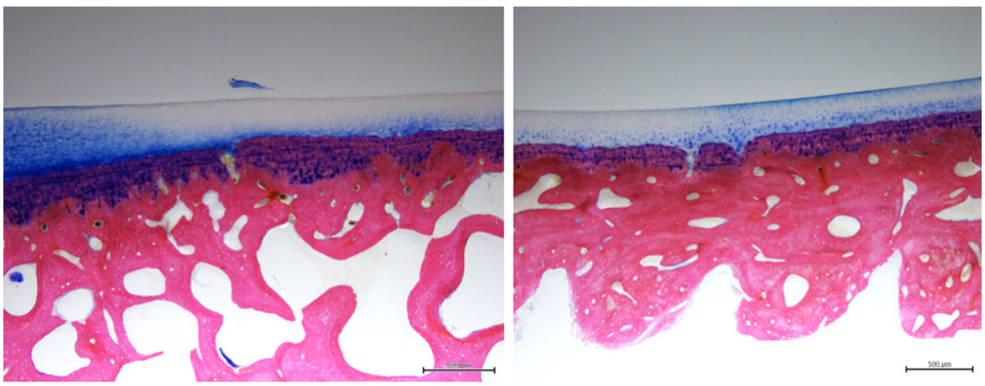

Fig. 4 Higher magnification of Fig. 3a (control) and 3b (treatment group)

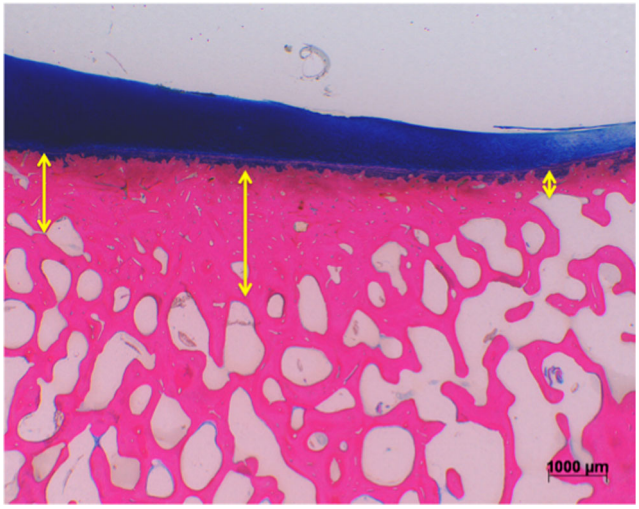

Fig. 5 Calculation of the subchondral plate thickness: At the thickest area of the weight bearing zone (*middle*), at the lowest area (*right*) and in between (*left*)

young mature sheep, to assure that changes will only occur due to screw insertion and are not biased by the trauma, fracture reduction or pre-existing osteoarthritis.

This study has the following drawbacks: We investigated an animal model, which is always limited regarding physiology, size and weight bearing of the cartilage and subchondral plate. Nevertheless, the anatomy of sheep joints is comparable to human joints and therefore an ideal experimental model for studying a range of orthopaedic conditions and treatments [30, 31]. With an average weight of 62 ± 5 kg a similar load to the joint as in humans can be assumed. An investigation period of two- and four-months follow up was chosen related to the following studies which investigated osteoarthritic changes after meniscectomy [31]. In canine, osteoarthritic changes after meniscectomy are described within three months [32, 33]. Within the four-month period no significant cartilage alterations were investigated; however, periimplant sclerosis, in particular next to or within the subchondral plate might, after a longer follow up, lead to consecutive cartilage damage. In this study design we simulated a conventional percutaneous proximal tibia osteosynthesis [34–36]. Instead of using two screws we only inserted one screw because of the following reason: As the size of the sheep knee is one third of the human knee the placement of a 3.5-mm diameter screw was chosen in this study to simulate similar conditions as in human proximal tibia osteosynthesis, where two times 6.5-mm screws are used. With the development of anatomic plate designs for joint fractures, different approaches with a high amount of subchondral metalwork are proposed, for example, for the proximal tibia fracture: four small fragment screws with a 3.5-mm diameter or two 4.5-mm locking screws in the less invasive stabilization system (LISS, De Puy Synthes Inc., Brüttisellen, Switzerland). Similar examples exist for distal radius [37] and proximal humerus [15] fractures. Therefore a large volume of the subchondral bone needs to be removed and is replaced by metalwork. These different volumes of metal could lead to different results and should be investigated further.

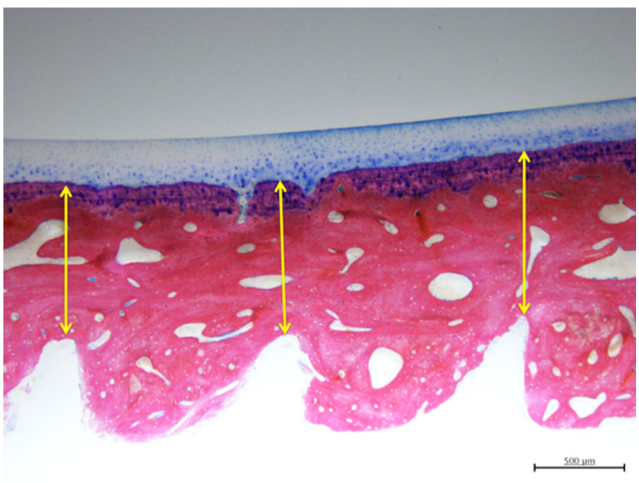

Fig. 6 Periimplant seam was included in the calculation of the subchondral plate in case it could not be differentiated

Conclusion

In conclusion we could show that single subchondral screw placement did not induce pathological reactions in the overlying cartilage layers after two- and four-month follow up. Sclerotic reaction next to the implant was observed. As to what extends these reactions and has an effect on the cartilage when implant placement occurs within the subchondral plate should be investigated further. The advantage of subchondral screw abutment is for the surgeon indispensable; first histological results did not show major complications.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Ethical approval All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. This study was performed in an AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) approved laboratory, according to the Swiss animal welfare regulations and approved by the ethical committee of the canton Graubünden, Switzerland (No. 2012_29).

Informed consent Informed consent was obtained from all individual participants included in the study.

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